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10/539,954	06/17/2005	Oliver Schmitz	13195-00006-US	8865

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
06/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,954	SCHMITZ ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-17,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-17 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 4-5, 7-17, and 26-27 are currently pending.

In response to a previous Office action, a non-final action (mailed on September 7, 2007), Applicants filed a response and amendment received on March 7, 2008, amending claims 1-2, 4-5, 7-17, cancelling claims 3, 6, and 18-25, and adding new claims 26-27 is acknowledged. New claim 27 recites the subject matter of Group V of the restriction requirement set forth on 11/3/2006 and thus is also withdrawn as reciting a nonelected invention.

Claims 1-2, 4-5, 7-17, and 26 are under consideration and are present for examination.

Applicants' arguments filed on March 7, 2008, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Maintained-Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Previous rejection of claim 5 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "negligible reduction" in the context of threonine degrading activity is maintained and claim 26 is included in this rejection. Applicants argue that the specification has clear definition of this phrase. While, the specification at page 45 defines "negligible reduction" means 10-40% reduction of a polypeptide having threonine degrading activity, a 40% reduction

is well outside any reasonable meaning of the word "negligible". While applicants may be their own lexicographers they cannot define a term as completely contrary to its standard meaning.

Maintained - Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous Claims 1-2, 4, and 7-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. This rejection has been discussed at length in the previous office action. The rejection is maintained for the following reasons.

Claims 1-2, 4 and 7-17 are directed to a process for preparing amino acids in transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding a threonine-degrading protein or increasing threonine-degradation (claim 1 and 2) having a consensus sequence of SEQ ID NO: 27 or 28 (claim 4), wherein said nucleic acid sequence depicted in SEQ ID NO: 1 encoding said protein of SEQ ID NO: 2.

Claims are drawn to a process of using any threonine-degrading enzyme whose structure is not fully described in the specification. No information, beyond the characterization of gene encoding threonine aldolase having a nucleic acid sequence of SEQ ID NO: 1 has been provided, which would indicate that they had possession of the claimed genus of any threonine degrading enzyme.

Applicants argue that the specification provide adequate written description for the following reasons. The specification provides at least three actual nucleic acids coding for threonine-degrading proteins (SEQ ID NO: 1, 13, and 15) and eleven actual amino acid sequences of threonine-degrading proteins (SEQ 1D NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 14, and 16). Furthermore; the specification describes several sequences identified by GenBank Accession number with threonine-degrading activity, which can be used in fine method of the invention, and applicants further argue that at least fourteen actual sequences is clearly a "representative" number of species of the genus and the Examiner has not provided reasons why it is not. Applicants also argue that the Examples 7-8 and I3 shows assays for determining activity and experiments showing activity. Because each embodiment need not be disclosed the specification provides a representative number of sequences under the standard *of Regents v. Lilly.* Additionally, the specification discloses a common structure for the threonine aldolases (see for example Figures 1 and 2). Therefore, the representative species described here provide identifiable structural and functional characteristics of the genus claimed.

Applicant's arguments and amendments to claims have been fully considered but are not deemed to be persuasive to overcome the rejection on written description issues.

The Examiner acknowledges applicants arguments that the specification provide 3 nucleic acid sequences encoding a protein having threonine degrading activity and several polypeptide sequences, however the claims still read on using any polypeptide having threonine degrading activity having no structural feature. Therefore, recited species would be representative of the entire genus. Regarding Applicants argument that claims provide consensus

sequence as identifying characteristics of said polypeptide, contrary to the applicants arguments, the Examiner interprets the consensus sequence having no structure at all because the consensus sequence of SEQ ID NO: 27, which has 62 amino acids, wherein 56 amino acids (X) are unknown out of 62 amino acids that does not provide any structural feature of said protein or any identifying characteristics such that one ordinary skilled in the art could practice the claimed invention with correlation with functional feature (threonine degrading activity), i.e. correlation of structure-function relationship of the claimed genus of protein for successfully practice the claimed invention, that is required for fulfilling written description requirements. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient structure and variety of species to reflect the representative structure variation within the genus.** Satisfactory disclosure of a representative structure and number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, cannot be achieved by

disclosing the structure of small portion of only one species within the genus. The genus of polypeptide having threonine degrading activity is structurally diverse as it broadly encompasses many mutants, and variants comprising threonine degrading activity having different structures. As such, the disclosure solely of functional features coupled with minor structural feature that may or may not present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus. Therefore, the rejection is maintained.

Previous rejection of claims 1-2, 4-5 and 7-17 under 35 U.S.C. 112, first paragraph on scope of enablement is maintained. This rejection has been discussed at length in the previous office action. The rejection is maintained for the following reasons.

The specification, while being enabling for a process for preparing amino acid methionine in transgenic organism, wherein the process comprises introduction of a nucleic acid sequence of SEQ ID NO: 1 encoding a threonine-degrading protein i.e. threonine aldolase of SEQ ID NO: 2 from S. cerevisiae, does not reasonably provide enablement for a process for preparing amino acids, wherein the process comprises introduction of any nucleic acid sequence encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequence encoding any protein having at least 70% homology to SEQ ID NO: 2 (claim 5). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use** the invention commensurate in scope with these claims.

Applicants argue that claims are directed to methods and not to the sequences themselves; thus, working examples for a specific sequence should not be required, there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. Applicants also argue that the specification provides detailed

description and guidance regarding at least three actual nucleic acids coding for threonine-degrading proteins (SEQ ID NO: 1, 13, and 15) and eleven actual amino acid sequences of threonine-degrading proteins (SEQ IDNO: 2, 3, 4, 51 6, 7, 8, 9, 10, 14, and 16). Furthermore, the specification describes several sequences identified by GenBank Accession number with threonine-degrading activity, which can be used in the method of the invention. Additionally, the specification discloses a common structure for the threonine aldolases and a common structure for the lysine decarboxylases. The specification shows in Examples 7-9 and 13 experiments showing activity and assays for determining activity. The specification additionally provides detailed guidance on how to identify variants of the sequences as well as how to test in routine assays for activity which is also well known to those skilled in the art as described in the specification. For example, the specification in Example 10 describes cloning of SEQ ID NO: 1 with the use of primers as well as the use of this method for the other sequences of the invention and Example 11 describes in detail the production of transgenic plants expressing SEQ ID NO: 1 as well as the other sequences of the invention. This detailed guidance and exemplification is applicable for any of the sequences used in the process. In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the present claims without undue experimentation.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection on scope of enablement issues. The examiner acknowledges the amendment to the claims and disclosing of 3 nucleic acid sequences of the polypeptide having threonine degrading activity and 11 amino acid sequences in the specification and some guidance in the working examples in the specification but disagrees with the applicants' contention that

the claimed invention is enabled for full scope claimed. Claims 1-2, and 4-5 are so broad as to encompass a process for preparing amino acids in a transgenic organism, wherein the process comprises introduction of a nucleic acid sequence encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequence encoding any protein having at least 70% identity to SEQ ID NO: 2, (30% non-identity for claim 5), i.e. applicants are claiming a method of using a polypeptide, wherein 116 amino acids are different out of 387 amino acids. Claims still read on using any nucleic acid having threonine degrading activity and the consensus sequence does not give any structural feature of said consensus sequence because said sequence has 56 unknown amino acids out of 62, which is enormously broad that does not provide any information to predict structural feature of the polypeptide having threonine degrading activity. Claims as written interprets any polypeptide, which comprises many mutants and variants having threonine degrading activity. One of ordinary skilled in the art would not know how to make the claimed invention without structural feature of the claimed nucleic acid molecule encoding polypeptide used in the claimed method which would require undue experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid sequences encoding any threonine-degrading protein (claims 1-2), or any nucleic acid sequences encoding any protein having at least 70% homology to SEQ ID NO: 2 (claim 5), which includes many mutants and variants used in the claimed method. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one threonine degrading protein i.e. threonine aldolase of SEQ ID NO: 2 encoded by SEQ ID NO: 1 used in the claimed method.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants useful as threonine aldolase having threonine degrading activity requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. For the rejected claims, this would clearly constitute **undue** experimentation. For example, Guo et al. (Protein tolerance to random amino acid change, Proc Natl Acad Sci U S A, 2004 Jun 22; 101(25): 9205-10, Epub 2004 Jun 14) teach that the percentage of random single substitution mutations which inactivate a protein for the protein 3-methyladenine DNA glycosylase is 34% and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 that the percentage of active mutants for multiple mutants appears to be exponentially related to this by the simple formula $(.66)^{x}$ X 100% where x is the number of mutations introduced. Applying this estimate to the instant protein 70% identity allows up to 116 mutations within the 387 amino acids of SEQ ID NO: 2 and thus only $(.66)^{116}$ X 100% or 1.2 x 10^{-19}% (i.e. ≅ 1 in several trillions) of random mutants having 70% identity would be active. Similarly at 95% identity 3.7 x 10^{-2}% (1 in 26). Current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within several hundred of inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within many millions or more as in the claims to 70% or less identity would not be possible. While enablement is not precluded by the necessity

for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Sufficient guidance has **not** been provided in the instant specification or in the prior art as at best art teaches to avoid changes of 5% of the structure of SEQ ID NO: 2 but does little to suggest what changes would be successful particularly for those enzymes having the substantial number of alterations necessary to produce a protein having 70% identity to SEQ ID NO: 2.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for preparing an amino acid in a transgenic organism, wherein the process comprises introduction of any nucleic acid sequence encoding any threonine-degrading protein, or any nucleic acid sequence encoding any protein having at least 70% identity to SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a process for preparing amino acids in a transgenic organism by introducing of a nucleic acid sequence encoding any threonine-degrading protein, or any nucleic acid sequence encoding any protein having at least 70% identity to SEQ ID NO: 2 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 1-2, 5, 7, 10, 14-16 under 35 U.S.C. 102(b) as being anticipated by Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS) is maintained and claim 26 is included in this rejection. Instant claims are drawn to a process for producing amino acid such as methionine, homoserine or lysine in transgenic organism including microorganism, wherein said microorganism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity.

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2, inherently a threonine degrading enzyme, wherein the process produces amino acid glycine. Monschau et al. further teach that the threonine degrading protein (threonine aldolase) comprises consensus sequences of SEQ ID NO: 27 and 28 (claim 2), which are 100% identical to SEQ ID NO: 27 and 28 of the instant application. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism.

Applicants argue that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Applicants' also argue that Monschau teaches riboflavin production *in A. gossypii* by enhancing the biosynthesis of the riboflavin precursor glycine through overexpression of the GLY1 gene from *A. gossypii. The* experiments described in Monschau resulted in increased riboflavin but only in the presence of threonine. Monschau does not teach a gene encoding threonine aldolase from S. *cerevisiae* but rather teaches isolation of *an A. gossypii* GLY1 gene and overexpression of this gene in the same fungal *strain A. gossypii* from which it was isolated (see Monschau abstract).

This is not found persuasive because indeed Monschau et al. teach GLY1 gene encoding threonine aldolase, which responsible for converting threonine to glycine (see p4283, line 3, abstract) and expression of GLY1 gene from genomic library of A. gossypii in M13, a S. cerevisiae strain (p. 4283, line 6-7, abstract) results in expression of threonine aldolase with specific activity of 25 mU/mg protein in S. cerevisiae strain M13, which is glycine auxotroph strain. Since, Glycine is the precursor of riboflavin, therefore, Monschau et al. also teach riboflavin, which is produced by biosynthesis of Glycine by GLY1 gene expression. Besides, Instant claims do not need the limitation of S. cerevisiae, wherein claim as written read on using any transgenic organism. Since, the gene of the reference is 99.8% identical to SEQ ID NO: 2, inherently a threonine degrading enzyme and Monschau et al. indeed teach expression of a plasmid Yep352, which encodes GLY1 gene and expressed in YM13, a Saccharomyces cerevisiae strain (see p4288, paragraph 3, line 11-16).

Applicants further argue that as recited in the specification and in the claims, the present invention provides a method for the production of methionine, homoserine and lysine in transgenic organisms by introducing and expressing a nucleic acid encoding a threonine-degrading protein and harvesting the transgenic organism or obtaining one or more of the amino acids. Monschau does not teach or describe that the GLY1 gene influences the production of methionine, homoserine and lysine in transgenic organisms and thus does not teach harvesting transgenic organisms or obtaining these amino acids.

This is not found persuasive because Monschau et al. indeed teach harvesting the transgenic microorganism to take dry weight of said transgenic microorganism (see p4284, Col 2, paragraph 6).

Therefore, Monschau et al. anticipate claims 1-2, 5, 7, 10, 14-16 and 26 of the instant application and the rejection is maintained as discussed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Previous rejection of Claim 11 under 35 U.S.C. 103(a) as obvious over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS) is maintained. This rejection has been discussed at length in the previous office action. The rejection is maintained for the following reasons.

Instant claims are drawn to a process for producing amino acid in transgenic organism including microorganism such as Saccharomyces cerevisiae, wherein said microorganism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity.

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase which degrade threonine, which is 99.8% identical to SEQ ID NO: 2 of the instant application, wherein the process produce amino acid glycine. Furthermore, Monschau et al. teach harvesting the

transgenic microorganism to take dry weight of said transgenic microorganism (see p4284, Col 2, paragraph 6). Although, Monschau et al. indirectly teach expression of an expression plasmid Yep352comprising GLY1 gene and expressed in M13, a strain of S. cerevisiae but not directly.

It would have been obvious to one of ordinary skill in the art to use fungal strain Saccharomyces instead of fungal strain A. gossypii, which is well-known host cell in the art.

One of ordinary skill in the art would have been motivated to do so because fungal strain Saccharomyces is readily available, well known, easy to grow and inexpensive fungal strain widely used in the art.

One of ordinary skill in the art would have a reasonable expectation of success because threonine aldolase gene is isolated from S. cerevisiae and using S. cerevisiae as host cell for producing enhanced threonine aldolase enzyme in order to producing enhanced glycine would be highly expected.

Applicants argue that Monschau does not teach, suggest, or reveal that the GLY1 gene influences the production of methionine, homoserine and/or lysine in transgenic organisms. Absence such teaching or suggestion in the art, it would not have been obvious to use a threonine-degrading gene in a process for production of methionine, homoserine and/or lysine in transgenic organisms with a reasonable expectation of success that a threonine-degrading gene when expressed would produce methionine, homoserine and/or lysine.

This is not found persuasive because as discussed above Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase which degrade threonine, which is 99.8% identical to SEQ ID NO: 2 of the instant application, wherein the process produce amino acid

glycine. In addition, all microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism. Furthermore, Monschau et al. teach harvesting the transgenic microorganism to take dry weight of said transgenic microorganism (see p4284, Col 2, paragraph 6).

Therefore, the rejection is maintained.

Withdrawn-Claim Rejections - 35 USC § 103

Previous rejection of Claims 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS) as applied to claims 1, 2, 5, 7-8, 10-11, and 14-16 above, and further in view of Castigioni et al. (US PGPUB 2005/0160500 A1, publication 7/21/2005, claim priority of 60/467,910 filed on 7/15/2003) is withdrawn in view of Applicants submission of foreign priority document in English language.

Conclusion

Status of the claims:

Claims 1-2, 4-5, 7-17, and 26-27 are pending.

Claim 27 is withdrawn.

Claims 1-2, 4-5, 7-17, and 26 are rejected.

No claims are allowed.

Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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